EXHIBIT 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: BRAJE et al.	)	
	)	Confirmation No.: 4358
Serial No. 10/552,842	)	
	)	Group Art Unit: 1624
Filed: August 22, 2006	)	
	)	Examiner: Emily B. Bernhardt

For : N-[(Piperazinyl)hetaryl]arylsulfonamide Compounds with Affinity for the Dopamine D_3 Receptor

DECLARATION UNDER 37 CFR §1.132

1. I, Wilfried M. Braje, Dr. rer. nat., a citizen of the Federal Republic of Germany and residing at Unter dem Hopfenberge 15, 31737 Rinteln, Germany, hereby declare as follows:

   I am a fully trained Chemist having studied Chemistry at the University of Hannover, Germany, from 1990 to 1996, at the University of Hawaii, USA, from 01/1994 to 10/1994 and at Stanford University, USA from 06/1995 to 04/1996. I received a Diploma Degree in 01/1996 by the University of Hannover, Germany. In 1999, I received the doctorate degree (Ph.D.) by the University of Hannover, Germany.

   I joined BASF Aktiengesellschaft, 67056 Ludwigshafen, Germany, in 2000 and relocated to Abbott GmbH&Co. KG, 67061 Ludwigshafen, Germany, in 2001. Since then, I have been working in the field of medicinal chemistry. I have read and fully understood US application Ser. No. 10/823,317 and I am familiar with the subject-matter disclosed and claimed therein;

2. I have read and fully understood the Office Action of March 24, 2008 and the references cited therein by the Examiner;

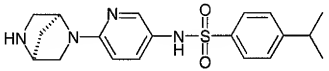
3. The following observations are made by me.

4. Supplementary Experimental Data

4.1 In order to provide further support for the compounds of formula I of claim 1, following additional synthesis examples, physicochemical and biological test data are presented.

4. 1.1 Synthesis examples

A) Synthesis of N-[(1S,4S)-6-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide



A.1) (1S,4S)-2-Benzyl-5-(5-nitro-pyridin-2-yl)-2,5-diaza-bicyclo[2.2.1]heptane

To 2-chlor-5-nitropyridine (666 mg, 4.2 mmol), (1S,4S)-2-benzyl-2,5-diazabicyclo[2.2.1]heptane (1.47 g, 4.2 mmol), benzyltrimethylammonium chloride (37 mg, 0.2 mmol) and potassium carbonate (2.322 g, 16.8 mmol) was added dimethylformamide (DMF) (20 ml). The reaction mixture was stirred for 1 h at room temperature. Water (200 ml) was added and the mixture was extracted twice with ethyl acetate (100 ml). The combined organic phases were washed with water and subsequently dried with sodium sulfate, filtered and concentrated in vacuo to give the desired crystalline product (1.21 g, 93 % yield).

MS [m+1]: 311.15

A.2) 6-((1S,4S)-5-Benzyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)pyridin-3-ylamine

(1S,4S)-2-Benzyl-5-(5-nitro-pyridin-2-yl)-2,5-diaza-bicyclo[2.2.1]heptane (1.2 g, 3.87 mmol) was dissolved in methanol (40 ml). Stannous dichloride (7.85 g, 34.8 mmol) was added, and the reaction mixture was stirred overnight at room temperature. Methanol was removed, the residue was treated with 1 N

aqueous sodium hydroxide to reach pH 9 and dichloromethane (50 ml) was added. The precipitated solid was filtered off and the aqueous phase was extracted twice with dichloromethane (100 ml). The combined organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the desired product (880 mg, 76 % yield).

MS [m+1]: 281.15

A.3) N-[6-((1S,4S)-5-Benzyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide

6-((1S,4S)-5-Benzyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)pyridin-3-ylamine (880 mg, 2.95 mmol), 4-isopropyl-benzene sulfonylchloride (582 µl, 3.25 mmol) and triethyl amine (1.23 ml, 8.86 mmol) were dissolved in THF (30 ml). The reaction mixture was stirred for 1 h at room temperature. The solvent was removed and water (100 ml) was added. The aqueous phase was extracted twice with diethyl ether. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to yield the product (1.14 g, 83 % yield).

MS [m+1]: 463.25

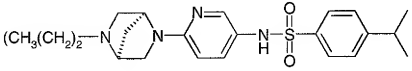
A.4) N-[(1S,4S)-6-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide

A mixture of N-[6-((1S,4S)-5-Benzyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide (1.14 g, 2.46 mmol) and 10 % palladium on carbon (50 mg) in a mixture of ethyl acetate (50 ml) and acetic acid (20 ml) was hydrogenated ovemight. The catalyst was filtered off, and the solvent was removed under vacuum. The residue was dissolved in distilled H_2O (50 ml) and extracted three times with ethyl acetate (150 ml). The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to yield the title compound (640 mg, 70 % yield).

MS [m+1]: 373.15

^{1}H-NMR (d_6-DMSO): δ = 7.65 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.15 (dd, 1H); 6.85 (d, 1H); 4.55 (s, 1H); 3.6 (s, 1H); 3.35 (dd, 1H); 3.05 (d, 1H); 2.95 (sept. 1H); 2.85 (d, 1H); 2.7 (d, 1H); 1.7 (d, 1H); 1.6 (d, 1H); 1.2 (d, 6H).

B) 4-Isopropyl-N-[6-((1S,4S)-5-propyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-benzenesulfonamide, hydrochloride



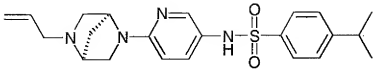
· HCl

N-[(1S,4S)-6-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide (300 mg, 0.81 mmol) and propionaldehyde (88 µl, 1.21 mmol) were dissolved in THF (20 ml). Acetic acid (63 µl, 1.21 mmol) and sodium trisacetoxyborohydride (341 mg, 1.21 mmol) were sequentially added to the reaction mixture and stirred for 30 minutes at room temperature. The reaction mixture was concentrated and the residue was dissolved in H_2O (50 ml) and twice extracted with ethyl acetate (50 ml). The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The residue was dissolved in diethyl ether (25 ml) and HCl in diethyl ether solution was added. The precipitate was collected to yield the desired product (235 mg, 62 % yield).

MS [m+1]: 415.25

H-NMR (d_6-DMSO): δ = 10.35 (bs, 1H); 10.05 (bs, 1H); 7.7 (s, 1H); 7.65 (d, 2H); 7.45 (d, 2H); 7.4 (s, 1H); 6.75 (m, 1H); 4.9 (s, 1H); 4.5 (s, 1H); 3.9 (d, 1H); 3.75 (d, 1H); 3.6 (d, 1H); 3.55 (m, 1H); 3.2 (m, 1H); 3.0 (m, 2H); 2.35 (d, 1H); 2.1 (d, 1H); 1.7 (m, 2H); 1.2 (d, 6H); 0.9 (t, 3H).

C) N-[6-((1S,4S)-5-Allyl-2,5-diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride



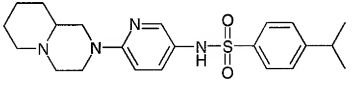
· HCl

N-[(1S,4S)-6-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide (300 mg, 0.81 mmol) was dissolved in DMF (10 ml). Allyl bromide (105 µl, 1.21 mmol) and triethyl amine (0.45 ml, 3.22 mmol) were added and the solution was stirred for 1 h at room temperature. Water (90 ml) was added and extracted twice with ethyl acetate (50 ml). The combined organic phases were washed with water (25 ml), and subsequently dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in diethyl ether (25 ml) and HCl in diethyl ether solution was added. The precipitate was collected to yield the desired product (272 mg, 70 % yield).

MS [m+1]: 413.25

^{1}H-NMR (d_6-DMSO): δ = 10.8 (bs, 1H); 10.05 (bs, 1H); 7.7 (d, 1H); 7.65 (d, 2H); 7.45 (d, 2H); 7.4 (d, 1H); 6.75 (m, 1H); 5.95 (m, 1H); 5.5 (m, 2H); 4.9 (s, 1H); 4.45 (s, 1H); 3.95 (m, 1H); 3.9 (d, 1H); 3.75 (m, 1H); 3.6 (d, 1H); 3.45 (m, 1H); 3.15 (d, 1H); 2.95 (m, 2H); 2.4 (d, 1H); 2.1 (d, 1H); 1.2 (d, 6H).

D) 4-Isopropyl-N-[6-(octahydro-pyrido[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-benzenesulfonamide



D.1) 2-(5-Nitro-pyridin-2-yl)-octahydro-pyrido[1,2-a]pyrazine

2-Chlor-5-nitropyridine (1.13 g, 7.13 mmol) and potassium carbonate (1.97 g, 14.26 mmol) were dissolved in DMF (10 ml) and stirred for 30 minutes at 0 °C. 1,4-Diazabicyclo[4.4.0]decane was added and the reaction was stirred at room

temperature overnight. The reaction mixture was concentrated and the residue was dissolved in H_2O (50 ml) and twice extracted with diethyl ether (50 ml). The combined organic phases were washed twice with water and subsequently dried with sodium sulfate, filtered and concentrated in vacuum to give the desired product (1.87 g, 100 % yield).

MS [m+1]: 263.15

D.2) 6-(Octahydro-pyrido[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine

2-(5-Nitro-pyridin-2-yl)-octahydro-pyrido[1,2-a]pyrazine (1.87 g, 7.12 mmol) was dissolved in methanol (50 ml), stannous dichloride was added (14.46 g, 64.1 mmol), and the reaction mixture was stirred at reflux for 3 h. Methanol was removed, and the residue was treated with 1 N aqueous sodium hydroxide to reach pH 9. Ethyl acetate was added and the precipitated solid was filtered off. The aqueous phase was extracted three times with dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the desired product (1.42 g, 86 % yield).

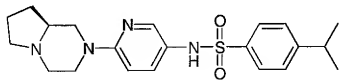
D.3) 4-Isopropyl-N-[6-(octahydro-pyrido[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-benzenesulfonamide

6-(Octahydro-pyrido[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine (300 mg, 1.29 mmol, 4-isopropyl-benzene sulfonylchloride (243 µl. 1.36 mmol) and triethyl amine (0.54 ml, 3.87 mmol) were dissolved in 10 ml THF. The reaction mixture was stirred overnight at room temperature. The solvent was removed and 100 ml water was added. The aqueous phase was extracted twice with diethyl ether. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel chromatography with cyclohexane/ethyl acetate (60-80%) as eluent, yielding the purified product (385 mg, 72 %).

MS [m+1]: 415.15

^{1}H-NMR (d_6-DMSO): δ = 7.7 (s, 1H); 7.65 (d, 2H); 7.4 (dd, 2H); 7.35 (d, 1H); 6.55 (d, 1H); 4.05 (m, 2H); 3.05-2.8 (m, 4H); 2.6 (t, 1H); 2.25 (m, 1H); 2.05 (m, 1H); 1.95 (m, 1H); 1.8 (s, 1H); 1.65 (m, 4H); 1.3 (m, 7H).

E) N-[(S)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride



· HCl

E.1) (S)-2-(5-Nitro-pyridin-2-yl)-octahydro-pyrrolo[1,2-a]pyrazine

2-Chlor-5-nitropyridine (1.256 g, 7.92 mmol) and potassium carbonate (2.19 g, 15.85 mmol) were dissolved in DMF (10 ml) and stirred for 30 minutes at 0 °C. (S)-1,4-Diazabicyclo[4.3.0]nonane was added and the reaction was stirred at room temperature overnight. The reaction mixture was concentrated and the residue was dissolved in H_2O (50 ml) and twice extracted with diethyl ether (50 ml). The combined organic phases were washed twice with water and subsequently dried with sodium sulfate, filtered and concentrated in vacuum to give the desired product (1.84 g, 94 % yield).

MS [m+1]: 249.15

E.2) (S)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine

(S)-2-(5-Nitro-pyridin-2-yl)-octahydro-pyrrolo[1,2-a]pyrazine (1.84 g, 7.41 mmol) was dissolved in methanol (50 ml), stannous dichloride was added (15.05 g, 66.7 mmol), and the reaction mixture stirred at reflux for 3 h. Methanol was removed, and the residue was treated with 1 N aqueous sodium hydroxide to reach pH 9. Ethyl acetate was added and the precipitated solid was filtered off. The aqueous phase was extracted three times with dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the desired product (1.36 g, 84 % yield).

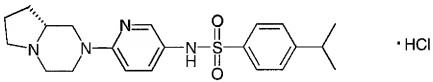
E.3) N-[(S)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride

(S)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine (400 mg, 1.83 mmol), 4-isopropyl-benzene sulfonylchloride (345 µl, 1.92 mmol) and triethyl amine (0.77 ml, 5.5 mmol) were dissolved in 10 ml THF. The reaction mixture was stirred overnight at room temperature. The solvent was removed and 100 ml of water were added. The aqueous phase was extracted twice with diethyl ether. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel chromatography with cyclohexane/ethyl acetate (30 %) and ethyl acetate/methanol (5 %) as eluent. The residue was dissolved in dichloromethane (5 ml) and HCl in diethyl ether solution was added. The precipitate was collected to yield the desired product (30 mg, 4 % yield).

MS [m+1]: 401.25

^{1}H-NMR (d_6-DMSO): δ = 11.3/11.05 (bs, 1H); 9.95 (s, 1H); 7.8/7.75 (s, 1H); 7.65 (d, 2H); 7.45 (d, 2H); 7.35 (m, 1H); 6.9/6.85 (d, 1H); 4.6/4.35 (d, 1H); 3.95 (m, 1H); 3.8-3.65 (m, 2H); 3.6-2.95 (m, 5H); 2.2-1.85 (m, 3H); 1.75 (m, 1H); 1.2 (m, 7H).

F) N-[(R)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride



· HCl

F.1) (R)-2-(5-Nitro-pyridin-2-yl)-octahydro-pyrrolo[1,2-a]pyrazine

2-Chlor-5-nitropyridine (600 mg, 4.75 mmol) and potassium carbonate (1.314 g, 9.51 mmol) were dissolved in DMF (10 ml) and stirred for 30 minutes at

0°C. (R)-1,4-Diazabicyclo[4.3.0]nonane was added and the reaction was stirred for 3 h at room temperature. The reaction mixture was concentrated and the residue was dissolved in H_2O (50 ml) and three times extracted with ethyl acetate (50 ml). The combined organic phases were washed twice with water and subsequently dried with sodium sulfate, filtered and concentrated in vacuum to give the desired product (1.1 g, 93 % yield).

MS [m+1]: 249.15

F.2) (R)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine

(R)-2-(5-Nitro-pyridin-2-yl)-octahydro-pyrrolo[1,2-a]pyrazine (1.1 g, 4.43 mmol) was dissolved in methanol (50 ml), stannous dichloride was added (9 g, 39.87 mmol), and the reaction mixture was stirred at reflux for 3 h. Methanol was removed, and the residue was treated with 1 N aqueous sodium hydroxide to reach pH 9. Ethyl acetate was added and the precipitated solid was filtered off. The aqueous phase was extracted three times with dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the desired product (1.12 g, 80 % purity, 93 % yield).

MS [m+1]: 219.15

F.3) N-[(R)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide, hydrochloride

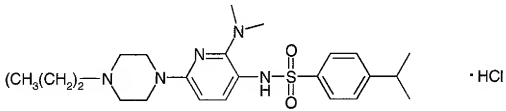
(R)-6-(Hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-pyridin-3-ylamine (400 mg, 80 % purity, 1.47 mmol), 4-isopropyl-benzene sulfonylchloride (263 µl. 1.47 mmol) and triethyl amine (0.61 ml, 4.4 mmol) were dissolved in 10 ml THF. The reaction mixture was stirred overnight at room temperature. The solvent was removed and 100 ml of water were added. The aqueous phase was extracted twice with diethyl ether. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel chromatography with ethyl acetate/methanol (5 %) as eluent. The residue was dissolved in

dichloromethane (5 ml) and HCl in diethyl ether solution was added. The precipitate was collected to yield the desired product (150 mg, 23 % yield).

MS [m+1]: 401.25

^{1}H-NMR (d_6-DMSO): δ = 11.3/11.05 (bs, 1H); 9.95 (s, 1H); 7.8/7.75 (s, 1H); 7.65 (d, 2H); 7.45 (d, 2H); 7.35 (d, 1H); 6.9/6.8 (d, 1H); 4.6/4.35 (d, 1H); 3.8-2.95 (m, 8H); 2.2-1.85 (m, 3H); 1.75 (m, 1H); 1.2 (m, 7H).

G) N-[2-Dimethylamino-6-(4-propyl-piperazin-1-yl)-pyridin-3-yl]-4-isopropyl-benzensulfonamide, hydrochloride



G.1) 1-Benzyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine and 1-Benzyl-4-(6-chloro-3-nitro-pyridin-2-yl)-piperazine

2,6-Dichlor-3-nitropyridine (1.0 g, 4.77 mmol) was dissolved in DMF (50 ml), benzylpiperazine (840 mg, 4.77 mmol) was added and the reaction was stirred overnight at room temperature. To the reaction mixture was added water (250 ml) and NaOH solution. The aqueous phase was extracted twice with ethyl acetate. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel chromatography with cyclohexane/ethyl acetate (5%-15%) as eluent to yield 1-benzyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine (200 mg, 13 % yield) and of 1-benzyl-4-(6-chloro-3-nitro-pyridin-2-yl)-piperazine (900 mg, 57 % yield).

1-Benzyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine

MS [m+1]: 333.05

^{1}H-NMR (d_6-DMSO): δ [ppm] 8.3 (d, 1H); 7.4-7.25 (m, 5H); 6.95 (d, 1H); 3.75 (bs, 4H); 3.55 (s, 2H); 2.5 (m, 4H).

1-Benzyl-4-(6-chloro-3-nitro-pyridin-2-yl)-piperazine

MS [m+1]: 333.05

^{1}H-NMR (d_6-DMSO): δ [ppm] 8.3 (d, 1H); 7.35 (m, 4H); 7.3 (m, 1H); 6.9 (d, 1H); 3.55 (s, 2H); 3.4 (bs, 4H); 2.5 (m, 4H).

G.2) [6-(4-Benzyl-piperazin-1-yl)-3-nitro-pyridin-2-yl]-dimethyl-amine

1-Benzyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine (200 mg, 0.60 mmol) was dissolved in THF (10 ml), a 2 molar solution of dimethylamine in THF (750 µl, 1.5 mmol) was added and the reaction was stirred overnight at room temperature. The solvent was removed and water (50 ml) was added. The aqueous phase was extracted twice with ethyl acetate. The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to yield the desired product (220 mg).

MS [m+1]: 342.15

G.3) 6-(4-Benzyl-piperazin-1-yl)-N*2*,N*2*-dimethyl-pyridine-2,3-diamine

[6-(4-Benzyl-piperazin-1-yl)-3-nitro-pyridin-2-yl]-dimethyl-amine (220 mg, 0.64 mmol) was dissolved in methanol (50 ml), stannous dichloride was added (1.31 g, 5.80 mmol), and the reaction mixture was stirred at reflux for 17 h. Methanol was removed, and the residue was treated with 1 N aqueous sodium hydroxide to reach pH 9. Ethyl acetate was added and the precipitating solid was filtered off. The aqueous phase was extracted with ethyl acetate. The combined organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the desired product (210 mg, 95 % purity, 99 % yield).

MS [m+1]: 312.25

G.4) N-[6-(4-Benzyl-piperazin-1-yl)-2-dimethylamino-pyridin-3-yl]-4-isopropyl-benzensulfonamide

6-(4-Benzyl-piperazin-1-yl)-N*2*,N*2*-dimethyl-pyridine-2,3-diamine (210 mg, 95 % purity, 0.64 mmol), 4-isopropyl-benzene sulfonylchloride (115 µl. 0.64 mmol) and triethyl amine (0.27 ml, 1.92 mmol) were dissolved in 25 ml THF. The reaction mixture was stirred for 7 h at 50°C. 4-Isopropyl-benzene sulfonylchloride (33 µl. 0.19 mmol) was added and the reaction mixture was stirred at room temperature overnight. The solvent was removed and aqueous NaOH solution was added. The aqueous phase was extracted twice with ethyl acetate. The combined organic phases were extracted once with 1 N HCl solution. The acidic aqueous phases was made alkaline with NaOH and then extracted twice with ethyl acetate. These two organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to give the crude product (130 mg, 80 % purity, 33 % yield).

MS [m+1]: 494.25

G.5) N-(2-Dimethylamino-6-piperazin-1-yl-pyridin-3-yl)-4-isopropyl-benzensulfonamide

A mixture of N-[6-(4-Benzyl-piperazin-1-yl)-2-dimethylamino-pyridin-3-yl]-4-isopropyl-benzensulfonamide (130 mg, 0.21 mmol) and 10 % palladium on carbon (10 mg) in a mixture of ethyl acetate (20 ml) and acetic acid (5 ml) was hydrogenated overnight. Further quantities of 10 % palladium on carbon and acetic acid (2 ml) were added. The catalyst was filtered off, and the solvent was removed under vacuum. The residue was treated with aqueous 1 N NaOH solution and extracted twice with ethyl acetate (100 ml). The organic phases were combined, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure to yield the product. The crude product was purified by silica gel chromatography to give the desired product (23 mg, 27 % yield).

MS [m+1]: 404.15

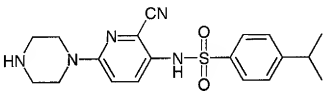
G.6) N-[2-Dimethylamino-6-(4-propyl-piperazin-1-yl)-pyridin-3-yl]-4-isopropyl-benzensulfonamide, hydrochloride

N-(2-Dimethylamino-6-piperazin-1-yl-pyridin-3-yl)-4-isopropyl-benzensulfonamide (23 mg, 0.06 mmol) and propionaldehyde (4 µl, 0.06 mmol) were dissolved in THF (5 ml). Acetic acid (5 µl, 0.09 mmol) and sodium trisacetoxyborohydride (18 mg, 0.09 mmol) were sequentially added to the reaction mixture and stirred for 1 h at room temperature. The reaction mixture was concentrated and the residue was dissolved in aqueous $NaHCO_3$ solution and extracted with diethyl ether. The organic phases were dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The residue was dissolved in diethyl ether (25 ml) and HCl in diethyl ether solution was added. The precipitate was collected to yield the desired product (19 mg, 69 % yield).

MS [m+1]: 446.25

^{1}H-NMR (d_6-DMSO): δ [ppm] 10.8 (bs, 1H); 9.2 (bs, 1H); 7.6 (d, 2H); 7.45 (d, 2H); 6.7 (d, 1H); 6.15 (bs, 1H); 4.25 (d, 2H); 3.5 (d, 2H); 3.25 (t, 2H); 3.0 (m, 5H); 2.9 (s, 6H); 1.75 (m, 2H); 1.2 (d, 6H); 0.9 (t, 3H).

H) N-(2-Cyano-6-piperazin-1-yl-pyridin-3-yl)-4-isopropyl-benzenesulfonamide



H.1) 4-(6-Cyano-5-nitro-pyridin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester

The compound was prepared from piperazine-1-carboxylic acid tert-butyl ester and 6-chloro-3-nitro-pyridine-2-carbonitrile by the method described for Example 1 of the present application . Yield: 6.9 g (77%).

ESI-MS: 234.5 $[M+H - Boc]^+$, 334.2 $[M+H]^+$

^{1}H-NMR (DMSO, 400 MHz): δ [ppm] 1.47 (s, 9H), 3.57 (m, 4H), 3.80 (m, 4H), 6.77 (d, 1H), 8.30 (d, 1H).

H.2) 4-(5-Amino-6-cyano-pyridin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester

The compound was prepared by reduction of 4-(6-cyano-5-nitro-pyridin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester by the method described for Example 1 of the present application. Yield: 5.60 g (90%).

ESI-MS: 204.1 $[M+H - Boc]^+$, 304.1 $[M+H]^+$

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] 1.47 (s, 9H), 3.32 (m, 4H), 3.50 (m, 4H), 3.93 (s, 2H), 6.81 (d, 1H), 7.02 (d, 1H).

H.3) 4-[6-Cyano-5-(4-isopropyl-benzenesulfonylamino)-pyridin-2-yl]-piperazine-1-carboxylic acid tert-butyl ester

The compound was prepared from 4-(5-amino-6-cyano-pyridin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester and 4-isopropyl-benzenesulfonyl chloride by the method described for Example 1 of the present application. Yield: 0.26 g (81%).

MS (ESI) m/z: 430.2 $[M+H - tBu]^+$

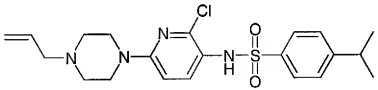
H.4) N-(2-Cyano-6-piperazin-1-yl-pyridin-3-yl)-4-isopropyl-benzenesulfonamide

The compound was prepared by acidic deprotection of 4-[6-cyano-5-(4-isopropyl-benzenesulfonylamino)-pyridin-2-yl]-piperazine-1-carboxylic acid tert-butyl ester by the method described for Example 1 of the present application. Yield: 0.12 g (88%).

ESI-MS: 386.1 $[M+H]^+$

^{1}H-NMR ($CDCl_3$, 400 MHz): δ [ppm] 1.21 (d, 6H), 2.98 (m, 1H), 3.14 (m, 4H), 3.70 (m, 4H), 7.17 (m, 2H), 7.46 (d, 2H), 7.52 (d, 2H), 9.00 (br s, 1H), 10.20 (br s, 1H).

I) N-[6-(4-Allyl-piperazin-1-yl)-2-chloro-pyridin-3-yl]-4-isopropyl-benzenesulfonamide



I.1) 1-Allyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine

The compound was prepared from piperazine-1-carboxylic acid tert-butyl ester and 2,6-dichloro-3-nitro-pyridine by the method described for Example 1 of the present application. Yield: 11.0 g (93%).

ESI-MS: 243.1 $[M+H - Boc]^+$, 287.0 / 289.0 $[M+H - tBu]^+$

^{1}H-NMR (DMSO, 400 MHz): δ [ppm] 1.42 (s, 9H), 3.37 (m, 4H), 3.46 (m, 4H), 6.92 (d, 1H), 8.30 (d, 1H).

I.2) 6-(4-Allyl-piperazin-1-yl)-2-chloro-pyridin-3-ylamine

The compound was prepared by reduction of 1-allyl-4-(6-chloro-5-nitro-pyridin-2-yl)-piperazine by the method described for Example 1 of the present application. Yield: 2.22 g (94%)

ESI-MS: 253.1 $[M+H]^+$

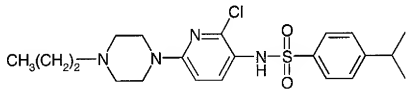
I.3) N-[6-(4-Allyl-piperazin-1-yl)-2-chloro-pyridin-3-yl]-4-isopropyl-benzenesulfonamide

The compound was prepared from 6-(4-allyl-piperazin-1-yl)-2-chloro-pyridin-3-ylamine and 4-isopropyl-benzenesulfonyl chloride by the method described for Example 1 of the present application. Yield: 1.96 g (65%).

ESI-MS: 435.1 $[M+H]^+$

^{1}H-NMR (DMSO): δ [ppm] 1.20 (m, 6H), 2.92 (m, 3H), 3.25 (m, 4H), 3.57 (m, 2H), 3.73 (m, 2H), 5.51 (m, 2H), 6.02 (m, 1H), 7.00 (d, 1H), 7.32 (d, 1H), 7.43 (d, 2H), 7.66 (d, 2H), 9.75 (br s, 1H).

J) N-[2-Chloro-6-(4-propyl-piperazin-1-yl)-pyridin-3-yl]-4-isopropyl-benzenesulfonamide

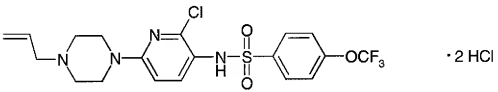


The compound was prepared by reduction of N-[6-(4-allyl-piperazin-1-yl)-2-chloro-pyridin-3-yl]-4-isopropyl-benzenesulfonamide by the method described for Example 17 of the present application. Yield: 0.20 g (46%).

ESI-MS: 437.1 $[M+H]^+$

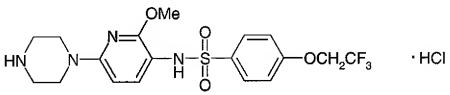
According to the above procedures, the following compounds were synthesized.

K) N-[2-Chloro-6-(4-allyl-piperazin-1-yl)-pyridin-3-yl]-4-trifluoromethoxy-benzenesulfonamide, dihydrochloride



MS of the dihydrochloride: 549.8

L) N-[2-Methoxy-6-(piperazin-1-yl)-pyridin-3-yl]-4-(2,2,2-trifluoroethoxy)-benzenesulfonamide, hydrochloride



MS: 482.9

4.1.2 Biological investigations

The receptor binding studies were carried out according to the method described in the present invention. The results are given in following table.

Example	K_i (D_3) [nM]	K_i (D_2) [nM]	$K_i(D_2) / K_i(D_3)$
A	82.3		
B	16.9	517	31
C	11.1	191	17
D	11.2		
E	11.8	272	23
G	2.0	29.3	15
H	16	702	44
K	1.2		
L	3	298	99

As can be seen, the compounds have a good affinity and selectivity for the D_3 receptor.

5. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1101 of Title 18 of the US-code and that such willful false statements may jeopardize the validity of the above-identified patent issued thereon.

Ludwigshafen, September 19, 2008 .....Wilfried Braje.....
(Wilfried Braje)

PAS01#5198.1
IDKEF

EXHIBIT 2

eMolecules®

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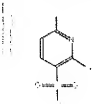
Draw Structure | Substructure | Exact molecule

ClS(=O)(=O)c1cccnc1 SEARCH

Advanced Search | Category Search | Preferences | Help

Searched **5.6M** structs from **16.2M** sources

Results 1-10 of ~10 (1.3 sec)



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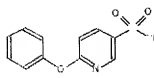

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Catalogue number: CC 19603, Catalogue: Screening Compounds, Supplier: Ambinter

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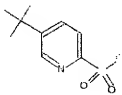
Catalogue number: CC 19603, Catalogue: Building Blocks, Supplier: Ryan



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Scientific Inc, CAS Number: 368869-91-4

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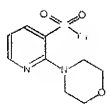

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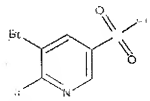

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Catalogue number: B682400, Catalogue: Building Blocks, Supplier: Toronto Research Chemicals, CAS Number: 216394-05-7

Catalogue number: YBB012117, Catalogue: Building Blocks, Supplier: Princeton BioMolecular Research

Catalogue number: OSSK_592577, Catalogue: Gold Collection, Supplier: Princeton BioMolecular Research

Catalogue number: L17015, Catalogue: Alfa Aesar, Lancaster and Avacado Compounds, Supplier: Alfa Aesar

Catalogue number: AKI-BBS-00001320, Catalogue: AKI (BBS,BBV) Building Blocks, Supplier: Ako Consulting and Solutions GmbH

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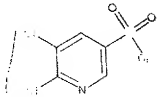

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Catalogue number: YBB011650, Catalogue: Building Blocks, Supplier: Princeton BioMolecular Research

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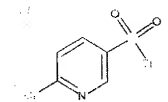

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Supplier: Otava

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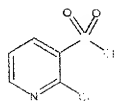

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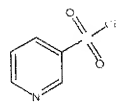

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Catalogue number: BOZH-0000053, Catalogue: Screening Compounds, Supplier: Chemical Technologies & Investigations, Ltd

Catalogue number: 019750, Catalogue: Matrix compounds, Supplier: Matrix Scientific

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Draw Structure | Substructure | Exact molecule

N1CC2NCC1C2 SEARCH

Advanced Search | Category Search | Preferences | Help

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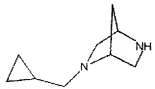
Results 1-10 of ~76 (0.5 sec)



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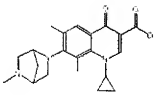

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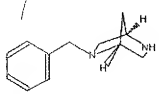

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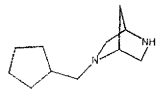

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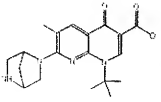

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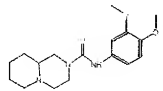

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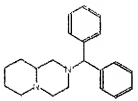

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Catalogue number: 011636, Catalogue: Matrix compounds, Supplier: Matrix Scientific

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Catalogue number: 032054, Catalogue: Building Blocks, Supplier: Oakwood Products Inc

Catalogue number: ZIB008615, Catalogue: Building Blocks, Supplier: Zelinsky Institute INC

Catalogue number: BAS 01217263, Catalogue: Screening Compounds, Supplier: Interchim

Catalogue number: OWH5-AL-24, Catalogue: Ost-West-Handels-gesellschaft

EXHIBIT 3

Catalog Name: MicroChemistry Building Blocks

Publication Date: 20 Oct 2003

Order Number: mch-bb-2003 11269

Chemical Name: Quinoxaline, decahydro-

Registry Number: 90410-24-5

Pricing: Quantity : 1 g-1 kg, Price: contact supplier

Company Info:
MicroChemistry Ltd.
Kosygina St. 4
Moscow, 119993
Russia
Phone: +7-(095)-518-9481
Fax: +7-(095)-518-9482
Email: sale@mch.ru
Web: http://www.mch.ru

Database: CHEMCATS (Copyright (C) 2006 ACS)

Catalog Name: Chemstep Product List

Publication Date: 17 May 2006

Order Number: 53753

Chemical Name: 1H-Cyclopentapyrazine, octahydro-

Registry Number: 154393-81-4

Pricing: Quantity : N/A, Price: contact supplier

Company Info: Chemstep
20 Avenue Victor Hugo
Carbon Blanc, 33560
France
Phone: +33 (0) 668 47 32 50
Fax: +33 (0) 540 00 33 30
Email: info@chemstep.com
Web: http://www.chemstep.com

Database: CHEMCATS (Copyright (C) 2006 ACS)

Answer 1:

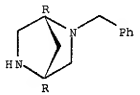
Catalog Name: ASDI Product List

Publication Date: 19 Jul 2006

Order Number: 500026459

Chemical Name: (1S,4S)-2-BENZYL-2,5-DIAZABICYCLO[2.2.1]HEPTANE DIHYDROBROMIDE

Registry Number: 134003-82-0



• 2 HBr

Pricing: Quantity : 1 g, Price: $95.00

Company Info: ASDI Inc
601 Interchange Blvd.
Newark, DE, 19711
USA
Phone: 302-266-6891
Phone: 1-888-577-ASDI (2734)
Fax: 302-266-8296
Email: customerservice@asdi.net
Web: http://www.asdi.net

Database: CHEMCATS (Copyright (C) 2006 ACS)

Answer 1:

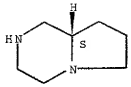
Catalog Name: Chemstep Product List

Publication Date: 17 May 2006

Order Number: 53784

Chemical Name: Pyrrolo[1,2-a]pyrazine, octahydro-, (8aS)-

Registry Number: 93643-24-4



Pricing: Quantity : N/A, Price: contact supplier

Company Info:
Chemstep
20 Avenue Victor Hugo
Carbon Blanc, 33560
France
Phone: +33 (0) 668 47 32 50
Fax: +33 (0) 540 00 33 30
Email: info@chemstep.com
Web: http://www.chemstep.com

Database: CHEMCATS (Copyright (C) 2006 ACS)

Answer 2:

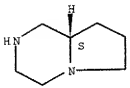
Catalog Name: CNH Product Catalog

Publication Date: 27 Jun 2006

Order Number: C-1311

Chemical Name: (S)-1,4-Diazabicyclo[4.3.0]nonane

Registry Number: 93643-24-4



Pricing:

Quantity : 1 G, Price: $240.00
Quantity : 5 G, Price: $960.00

Company Info:

CNH Technologies, Inc.
10A Henshaw Street
Woburn, MA, 01801
USA
Phone: (781) 933-0362
Fax: (781) 933-1839
Email: info@cnhtechnologies.com
Web: http://www.cnhtechnologies.com

Database:

CHEMCATS (Copyright (C) 2006 ACS)

Structure | Model | Prices | Catalog | Address

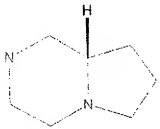
MDL ACD 2006.3

CAS# 93643-24-4 MF: $C_7H_{14}N_2$ MW: 126.2020

MFCD03787926 Name: (S)-1,4-DIAZABICYCLO[4.3.0]NONANE

Suppliers:
ABCR
ANASPEC
CNH-TECH

Structure:



H acceptors	H donors	MW(frag)	Torsional d.f.	Calc. logP	Violations
2	1	126	0	2	0

Structure | Model | Prices | Catalog | Address

MDL ACD 2006.3

MFCD00082600

CAS#

MF: $C_7H_{14}N_2$

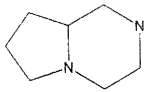
MW: 126.2020

Name: OCTAHYDRO-PYRROLO[1,2-A]PYRAZINE

Suppliers:

AKOS
ART-CHEM-BB
CHEMBRDG-BB
CHEMCOLLECT
FLUOCHEM
INTRCHM-BB
MATRIX
PRINCETON
TIMTEC-BB

Structure:



H acceptors	H donors	MW(frag)	Torsional d.f.	Calc. logP	Violations
2	1	126	0	2	0

Structure | Model | Prices | Catalog | Address

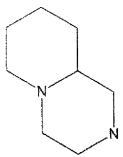
MDL ACD 2006.3

CAS# 5654-83-1 MF: $C_8H_{16}N_2$ MW: 140.2280

MFCD01098257 Name: (+/-)-1,4-DIAZABICYCLO[4.4.0]DECANE

Suppliers:
ABCR
AKOS
ANASPEC
ASINEX-REAG
CHEMCOLLECT
CNH-TECH
FLROCHEM
INTRCHM-BB
MATRIX

Structure:



H acceptors	H donors	MW(frag)	Torsional d.f.	Calc. logP	Violations
2	1	140	0	7	0